In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 08-0818V
(To be published[1])

RICHARD COOMBS and VILETTA COOMBS, natural parents and guardians of RWC, a minor,	*	
Petitioners,	*	Filed: April 8, 2014
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES	*	Vaccine Act Entitlement; Causation-in-fact; MMR-Varivax/ Autism Spectrum Disorder.
Respondent.	*	

Lawrence Gene Michel, Salina, Kansas, for Petitioners.
Traci R. Patton, U.S. Department of Justice, Washington, DC, for Respondent.

DECISION

HASTINGS, *Special Master*.

This is an action in which Petitioners, Richard and Viletta Coombs, seek an award under the National Vaccine Injury Compensation Program (hereinafter "the Program[2]), on account of their son RWC's autism spectrum disorder ("ASD"), that they believe was caused by one or both of a measles, mumps, rubella ("MMR") vaccination and a Varvivax vaccination, administered to their son on November 14, 2005. For the reasons set forth below, I conclude that Petitioners are not entitled to an award.

[1] Because I have designated this document to be published, this document will be made available to the public unless petitioners file, within fourteen days, an objection to the disclosure of any material in this decision that would constitute "medical files and similar files the disclosure of which would constitute a clearly unwarranted invasion of privacy." *See* 42 U.S.C. § 300aa-12(d)(4)(B); Vaccine Rule 18(b).

[2] The applicable statutory provisions defining the Program are found at 42 U.S.C. § 300aa-10 *et seq.* (2006 ed.). Hereinafter, for ease of citation, all "§" references will be to 42 U.S.C. (2006 ed.).

I

THE APPLICABLE STATUTORY SCHEME

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300 aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

In other cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In such instances, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. § 300aa-13(a)(1)(B); § 300aa-11(c)(1)(C)(ii). In such a situation, of course, the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. HHS*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines v. HHS*, 940 F.2d 1518, 1525 (Fed. Cir. 1991). The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1279; *Hines*, 940 F.2d at 1525. Under that standard, the petitioner must show that it is "more probable than not" that the vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause or even the predominant cause of the injury or condition, but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *Shyface v. HHS*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury;" the logical sequence must be supported by "reputable medical or scientific explanation, *i.e.*, evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. HHS*, 956 F.2d 1144, 1148 (Fed. Cir. 1992).

The *Althen* court also provided additional discussion of the "causation-in-fact" standard, as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally

> connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from *medical literature* supporting petitioner's causation contention, so long as the petitioner supplies the *medical opinion* of an expert. (*Id*. at 1279-80.) The court also indicated that, in finding causation, a Program fact-finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." (*Id*. at 1280.)

Since *Althen*, the Federal Circuit has addressed the causation-in-fact standard in several additional rulings, which have affirmed the applicability of the *Althen* test, and afforded further instruction for resolving causation-in-fact issues. In *Capizzano v. HHS*, 440 F.3d 1317, 1326 (Fed. Cir. 2006), the court cautioned Program fact-finders against narrowly construing the second element of the *Althen* test, confirming that circumstantial evidence and medical opinion, sometimes in the form of notations of treating physicians in the vaccinee's medical records, may in a particular case be sufficient to satisfy that second element of the *Althen* test. Both *Pafford v. HHS*, 451 F.3d 1352, 1355 (Fed. Cir. 2006), and *Walther v. HHS*, 485 F.3d 1146, 1150 (Fed. Cir. 2007), discussed the issue of which party bears the burden of ruling out potential non-vaccine causes. *DeBazan v. HHS*, 539 F.3d 1347 (Fed. Cir. 2008), concerned an issue of what evidence the special master may consider in deciding the initial question of whether the petitioner has met her causation burden. The issue of the temporal relationship between vaccination and the onset of an alleged injury was further discussed in *Locane v. HHS*, 685 F.3d 1375 (Fed. Cir. 2012), and *W.C. v. HHS*, 704 F.3d 1352 (Fed. Cir. 2013). *Moberly v. HHS*, 592 F.3d 1315 (Fed. Cir. 2010), concluded that the "preponderance of the evidence" standard that applies to Vaccine Act cases is the same as the standard used in traditional tort cases, so that *conclusive* proof involving medical literature or epidemiology is *not* needed, but demonstration of causation must be more than "plausible" or "possible." Both *Andreu v. HHS*, 569 F.3d 1367 (Fed. Cir. 2009), and *Porter v. HHS*, 663 F.3d 1242 (Fed. Cir. 2011), considered when a determination concerning an expert's credibility may reasonably affect the outcome of a causation inquiry. *Broekelschen v. HHS*, 618 F.3d 1339 (Fed. Cir. 2010), found that it was appropriate for a special master to determine the reliability of a diagnosis before analyzing the likelihood of vaccine causation. *Lombardi v. HHS*, 656 F.3d 1343 (Fed. Cir. 2011), and *Hibbard v. HHS*, 698 F.3d 1355 (Fed. Cir. 2012), both again explored the importance of assessing the accuracy of the diagnosis that supports a claimant's theory of causation. *Doe 11* v. HHS, 601 F.3d 1349 (Fed.Cir. 2010) and *Deribeaux v. HHS*, 717 F.3d 1363 (Fed. Cir. 2013), both discuss the burden of proof necessary to establish that a "factor unrelated" to a vaccine may have caused the alleged injury.

Another important aspect of the causation-in-fact case law under the Program concerns the factors that a special master should consider in evaluating the reliability of expert testimony and other scientific evidence relating to causation issues. In *Daubert v. Merrell Down Pharmaceuticals, Inc*., 509 U.S. 579 (1993), the Supreme Court listed certain factors that federal

trial courts should utilize in evaluating proposed expert testimony concerning scientific issues. In *Terran v. HHS*, 195 F.3d 1302, 1316 (Fed. Cir. 1999), the Federal Circuit ruled that it is appropriate for special masters to utilize *Daubert*'s factors as a framework for evaluating the reliability of causation-in-fact theories presented in Program cases.

II

PROCEDURAL HISTORY

On November 17, 2008, Petitioners filed, *pro se*, a "Short-Form Autism Petition for Vaccine Compensation" under the National Vaccine Injury Compensation Program, on behalf of their son, RWC. (*See* Petition ("Pet") at 1.) The case was originally assigned to Special Master Golkiewicz. (Notice of Assignment filed Nov. 17, 2008, ECF No. 2.)

Respondent's counsel filed a "Rule 4 Report" on December 18, 2008, noting inadequacies in the petition. (ECF No. 5.) On January 30, 2009, attorney Lawrence Michel filed a motion to substitute as counsel for the *pro se* Petitioners. (ECF No. 6.)

Petitioners filed RWC's medical records between April 24, 2009, and October 13, 2011. (*See* Exs. 1-50, 54.)[3]

On April 29, 2010, Petitioners filed a motion to remove their claim from the Omnibus Autism Proceeding (OAP).[4] (ECF No. 23.) Special Master Golkiewicz granted this motion on

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[3] Exhibits filed by Petitioners are identified by numbers. Exhibits filed by Respondent are identified by letter.

[4] The Omnibus Autism Proceeding was a special proceeding under the Vaccine Act in which three special masters addressed the *general issue* of whether certain vaccines can contribute to causing autism. On February 12, 2009, those three special masters separately issued decisions in the first three "test cases" in the OAP: *Cedillo v. HHS*, No. 98-916V, 2009 WL 331968 (Fed. Cl. Spec. Mstr. Feb. 12, 2009); *Snyder v. HHS*, No. 01-162V, 2009 WL 332044 (Fed. Cl. Spec. Mstr. Feb. 12, 2009); *Hazlehurst v. HHS*, No. 03-654V, 2009 WL 332306 (Fed. Cl. Spec. Mstr. Feb. 12, 2009). All three decisions determined that the evidence failed to demonstrate any general causal connection between the *MMR vaccine* and the development of autism spectrum disorders. These decisions were each subsequently affirmed, on appeal, by three different judges of the U.S. Court of Federal Claims. *Cedillo v. HHS*, 89 Fed. Cl. 158 (2009); *Snyder v. HHS*, 88 Fed. Cl. 706 (2009); *Hazlehurst v. HHS*, 88 Fed. Cl. 473 (2009). Subsequently, the two cases that were appealed to the U.S. Court of Appeals for the Federal Circuit, *Cedillo* and *Hazlehurst*, were again affirmed. *Cedillo v. HHS*, 617 F.3d 1328 (Fed. Cir. 2010); *Hazlehurst v. HHS*, 604 F.3d 1343 (Fed. Cir. 2010). (The *Snyder* case was not appealed to the Federal Circuit.) In March of 2010, the same three special masters issued opinions in three more OAP "test cases," this time rejecting the *second* causation theory presented in the OAP, that *thimerosal-containing vaccines* can cause autism. *King v. HHS*, No. 03-584V, 2010 WL 892296 (Fed. Cl. Spec. Mstr. Mar. 12, 2010); *Mead v. HHS*, No. 03-215V, 2010 WL 892248 (Fed. Cl. Spec. Mstr. Mar. 12, 2010); *Dwyer v. HHS*, No. 03-1202V, 2010 WL

May 10, 2010. (ECF No. 24.) Petitioners then filed an amended petition on September 17, 2010, alleging that the MMR and Varivax vaccines that RWC received on November 14, 2005, "aggravated [RWC's] underlying Complex I and III deficiencies related to mitochondrial disease, caused [RWC] to develop chronic illness, high fevers, become developmentally delayed, and develop features consistent with Autism Spectrum Disorder." (Amended Petition ("Amended Pet.") at 1.) The case was reassigned to me on February 11, 2011. (ECF No. 38.)

On April 13, 2011, Petitioners filed an expert report from J. Ivan Lopez, M.D., and his curriculum vitae ("CV"). (Exs. 51, 52.) Petitioners additionally filed supplemental expert reports from Dr. Lopez on June 29, 2011, and July 31, 2012. (Exs. 53, 55.)

On November 19, 2012, I conducted an evidentiary hearing in Washington, D.C. (*See* Transcript of Proceedings ("Tr."), ECF No. 61.) RWC's mother, Ms. Coombs, and Petitioners' expert Dr. Lopez testified for Petitioners; experts Dr. Korson and Dr. Wiznitzer testified for Respondent. (*Id.*)

On April 17, 2013, Petitioners' counsel filed their opening post-hearing brief. On July 17, 2013, Respondent's counsel filed a responsive post-hearing brief, and on September 16, 2013, Petitioners' counsel filed a reply brief.

III

STATEMENT OF FACTS

RWC was born healthy on July 6, 2004. (Exs. 1, 3, 13, 19, 39, 40.) He was discharged on July 8, 2004. (Ex. 13, p. 431.) It is noted in RWC's medical history that RWC was hospitalized shortly after being born, on account of dehydration due to poor "p.o. intake from being exclusively breast fed and needed to stay for two days." (Ex. 16, p. 628.)

RWC's immunization history began with administrations of DTaP on September 17, 2004, November 8, 2004, January 11, 2005, and February 9, 2006, OPV on September 17, 2004, November 8, 2004, and February 9, 2006; hepatitis B on July 6, 2004, August 5, 2004, and April 25, 2005; and Prevnar on September 17, 2004, November 8, 2004, January 11, 2005, and July 6, 2005. (Ex. 9, p. 282.)

On November 14, 2005, RWC's sixteen-month MMR and Varivax vaccinations were administered at the office of Dr. Brunnel. (Ex 34, p. 1622.) The record for that November 14 visit indicates that by this time RWC was experiencing oral and texture aversions. (*Id.*) During his next pediatrician visit, on December 1, 2005, RWC was noted to be "healthy appearing, happy and extremely active." (Ex. 9, p. 309) No fever is mentioned in RWC's December 1 medical record. (*Id.*)

892250 (Fed. Cl. Spec. Mstr. Mar. 12, 2010). None of those decisions were appealed. For further discussion of the OAP, *see Cedillo v. HHS*, 2009 WL 331968 at *8-11.

On December 19, 2005, RWC had a pediatric visit where he presented with decreased feeding, coughing, vomiting, stuffy nose, and a maximum temperature of 99-100 degrees.[5] (Ex. 16, pp. 705-06.) RWC was noted on December 20, 2005, to have the same aforementioned symptoms, alongside diarrhea and an elevated temperature around 102 degrees. (Ex. 16, p. 706.)

RWC experienced the same symptoms the next day on December 21, 2005, and was noted as unable to breathe through his nose and "cannot eat or drink; has had no liquid or solid intake, and his temperature was elevated to around 103 degrees." (Ex. 16, p. 706.) RWC was thereafter admitted to Tallahassee Memorial Hospital on that same day for a flu-like illness and dehydration. (Ex. 9, p. 351.) RWC's temperature then went up to 108 degrees, but then gradually abated; he was not treated with antibiotics. (*Id.,* pp. 351-52.) RWC was also noted to have "oral aversions" on that day. (*Id.*) RWC was thereafter discharged from Tallahassee Memorial Hospital on December 23, 2005, with a diagnosis of viral upper respiratory tract infection. (*Id*.)

In January 2006, it was noted, in RWC's medical history from Dr. Caudill at the Mayo Clinic, that RWC entered daycare for the first time during that month. (Ex. 22, p. 900.) The notes indicate that "he did not do very well any time thereafter. He continually becomes sick, and his mother describes these sicknesses as being characterized by frequent bouts of otitis media requiring antibiotic treatment." (*Id.*)

From this point forward, RWC amassed a lengthy medical history totaling in the thousands of pages, as the Coombs family expended a great amount of effort in seeking to diagnose and treat RWC's condition. Ms. Coombs testified extensively about this history, indicating that they saw more than 20 specialists on what she aptly described as a "scavenger hunt." (Tr. 34.) During this period RWC underwent a series of adenoidectomy and ear tube surgeries in an effort to address his recurrent ear infections and illnesses. (Ex. 22, p. 901; Ex. 16, p. 714.) Questions regarding whether RWC's developmental delays could be explained at least in part by possible hearing loss persisted during these years, while other explanations were also pursued. (*See, e.g.*, Ex. 17, p. 748; Tr. 37-41.)

A family service evaluation on February 7, 2006, noted that RWC "is showing significant delays in all areas other than physical development." (Ex. 34, p. 1976.) The evaluation note indicates that RWC's parents reported that RWC has been "lining up grains of rice, and lined up all his toys. They also reported that he will search the carpet for the tiniest piece of fuzz (lint), and will put it in his mouth." (*Id.*) This behavior was observed during the visit of February 7, 2006, when RWC picked up a hair off the couch and attempted to put it in his mouth. (*Id.*)

On February 6, 2007, a physician report from the Developmental Evaluation and Intervention Clinic stated that RWC had a history of sensory issues, which worsened after he began daycare about a year prior. (Ex. 24, p. 1017.) He was noted to use signs and words and point out to others what he wanted. (*Id.*) He was also noted to rub his face on the wall for

[5] Ms. Coombs testified that RWC experienced a fever "on or about the same day" he received his MMR and Varivax vaccinations. (Tr. 20-21) Ms. Coombs also offered testimony indicating that RWC experienced a fever in early December, around the 6th or 8th. (Tr. 24.) The fever recorded on December 19, however, is the earliest fever noted in RWC's medical records.

stimulation. (*Id.*) This report additionally states that on the Hawaii Early Learning Profile ("HELP") scale at age 31 months, RWC's corresponding developmental ages were as follows: regulatory/sensory organization -- 30-36 months; cognitive -- 19-24 months; language -- 12-15 months; social-emotional -- 18-24 months; gross motor -- 24-26 months; fine motor -- 18-24 months; and self-help -- 18-24 months. (Ex. 24, p. 1018.) For language, he used 1-3 words in his expressive vocabulary, and was beginning to use exclamatory expressions. (*Id.*, p. 1019.) He was not yet using 'dada,' 'mama,' or 'no,' specifically, and was not naming objects. (*Id.*) In the "wrap-up" portion of this report, the physician noted that there was a concern that RWC was on the autism spectrum. (*Id.*, p. 1020.)

On December 1, 2008, an evaluation at the Tridas Center for Child Development elicited a history of single word use and knowledge of shapes, numbers, and letters. (*See generally* Ex. 35.) RWC had immediate and delayed echolalia (repetition of words without comprehension), and his eye contact was variable. (Ex. 35, pp. 2079-80.) He did not play interactively with peers. (*Id.,* p. 2080.) He had unusual hand and finger movements, and was noted to have many autistic spectrum symptoms.[6] (*Id.*, p. 2081.)

Eventually, RWC was referred to Childhood Neurology in Atlanta, Georgia, where he was assessed for a possible mitochondrial disorder. (Tr. 48-50.) At Childhood Neurology, RWC was treated by Dr. Goldstein, but was sent to a specialist, Dr. Shoffner, for a determination as to whether he had a mitochondrial disorder. (Tr. 50-51.) Dr. Shoffner stated "I am NOT convinced that this patient has a mitochondrial disease. A single abnormality (abnormal enzymology) is not sufficient criteria for definitive diagnosis." (Ex 43, p. 2334.) A neurology follow-up on November 13, 2009, with Dr. Goldstein, listed relative deficiencies in Complex I and III, with ongoing metabolic/genetic testing by Dr. John Shoffner.

At the present time, RWC still continues to undergo treatment for his aforementioned symptoms. (Ex. 50, p. 51.)

IV

ISSUE TO BE DECIDED

In this case, Petitioners seek a Program award, contending that RWC's autism spectrum disorder was "caused-in-fact" or "aggravated" by the MMR and/or Varivax vaccinations administered to their son on November 14, 2005. After careful consideration, I conclude that they have failed to meet their burden.[7]

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[6] Because RWC's records are so extensive, it is impossible to fully catalog all of the various clinical observations they contain. Suffice it to say that these observations do not uniformly recognize RWC's condition as being ASD. I gloss over these distinctions, because the parties do not dispute that RWC does, in fact, suffer from an ASD.

[7] Petitioners have the burden of demonstrating the facts necessary for entitlement to an award by a "preponderance of the evidence." § 300aa-12(a)(1)(A). Under that standard, the existence of a fact must be shown to be "more probable than its nonexistence." *In re Winship*, 397 U.S. 358, 371 (1970) (Harlan, J., concurring).

Petitioners' theory of the case may be briefly summarized as follows. Petitioners contend that at the time of his MMR and Varivax vaccinations, RWC had an undiagnosed underlying mitochondrial disorder (specifically Complex I and Complex III deficiencies) and mild Autism Spectrum Disorder. They allege that it is more likely than not that febrile episodes provoked by RWC's MMR and Varivax vaccines "unmasked" the underlying mitochondrial disorder by virtue of excessive metabolic demands that RWC's system could not meet and overcome. As a result, RWC experienced autistic regression.

Respondent disagrees. Respondent contends that there is insufficient evidence to confirm a diagnosis of mitochondrial disease in RWC, and that there is a lack of temporal connection between RWC's immunizations and onset of his developmental issues.

V

SUMMARY OF EXPERT WITNESSES' QUALIFICATIONS AND OPINIONS

In this case, Petitioners presented an expert report and testimony from one medical expert, and Respondent presented expert reports and testimony from two medical experts. At this point, I will briefly summarize both the qualifications and the opinions of these expert witnesses.

A. Petitioners' expert

1. Dr. J. Ivan Lopez

Dr. J. Ivan Lopez attended La Salle University School of Medicine where he received a degree in medicine in 1982. (Ex. 52, p. 10.) He thereafter became a physician and surgeon at the National Autonomous University of Mexico in 1983. (*Id.*)

Dr. Lopez has extensive postgraduate experience and has held positions at Mercer University School of Medicine, the Ramadan Hand Institute, Organon Laboratories, Servimed Medical Group, and the "lo Octubre" Hospital in Mexico City. (Ex. 52, pp. 2-4.) From September to October 2005, Dr. Lopez was a visiting professor of neurology at the University of Montemorelos School of Medicine in Montemorelos, Nuevo Leon Mexico. (*Id.,* p. 2.) From 2008-2009, Dr. Lopez held positions as the Stroke Fellowship Director at the University of South Alabama, Clerkship Director at the University of South Alabama Department of Neurology, and the Director at the University of Alabama Stroke Center. (*Id.*) From 2009-2011, Dr. Lopez served as an Associate Professor of Pediatrics at the University of Alabama at Birmingham, Scientist to the University of Alabama Comprehensive Neuroscience Center, Associate Professor of Neurology, and Director of the Vascular Neurology Training Program. (*Id.*; Tr. 95.) He also served as the Clerkship Director at the University of Alabama at Birmingham, Department of Neurology from 2010-2011. (Ex. 52, p. 2; Tr. 96.)

Dr. Lopez was licensed to practice medicine in Mexico in 1986, received an Educational Commission for Foreign Medical Graduates ("ECFMG") certificate in 1991, received an

Alabama State Medical License in 1993, received a Florida Medical License in 1996, and received a Georgia Medical License in 2001. (Ex. 52, p. 15.) He was certified in Neurosonology by the American Society of Neuroimaging in 1995, the American Board of Psychiatry and Neurology in Child Neurology in 2000, and by the United Council for Neurologic Subspecialties in Headache Medicine in 2007. (*Id.*)

Additionally, Dr. Lopez was appointed as a Fellow of the American Academy of Neurology from 2006-2010. (Ex. 52, p. 17.) He has served on various medical committees and received the Army Achievement Medal for services rendered at Landstuhl Regional Medical Center during Operation Enduring Freedom and Operation Iraqi Freedom in 2006. (Ex. 52, p. 17-18; Tr. 95-96.) Dr. Lopez maintains a clinical practice in pediatric neurology, but does not treat any patients with mitochondrial disorder as part of that clinical practice. (Tr.133.)

From 1995- 2009, Dr. Lopez served as a co-investigator in many scientific trials involving neurological issues, and Dr. Lopez has 13 peer-reviewed publications listed on his *curriculum vitae* ("CV"). (Ex. 52, pp. 14-15.)

2. Summary of opinion of Petitioners' expert

Dr. Lopez testified that by the nature of mitochondrial diseases, patients may be asymptomatic until their metabolic system is taxed in excess, as in strenuous exercise, febrile illness, and/or any concomitant condition whereby the patient must provide extra energy to meet higher metabolic demands. (Ex. 51, p. 3; Tr. 99-100.) Dr. Lopez opined that this is exactly what happened to RWC, arguing that although the vaccines received on November 14, 2005, did not produce Complex I and Complex III mitochondrial deficiencies, it is more likely than not that the febrile episodes allegedly provoked by these vaccines *unmasked* RWC's underlying condition, by virtue of excessive metabolic demands that his system could not meet and overcome. (Ex. 51, p. 3.) As a result, RWC developed pervasive developmental delay. (*Id*.)

In his supplemental expert report, Dr. Lopez was asked to specify (1) which vaccine (MMR or Varivax) caused RWC's febrile episodes; (2) when those episodes occurred; and (3) *how* those episodes aggravated, or "unmasked," RWC's underlying mitochondrial disorder. (Ex. 53, p. 2.) Dr. Lopez responded that as to the first question, both vaccines could have been responsible for the febrile episodes previously mentioned. (*Id.*) In regard to the second question, *two weeks* after he received his vaccinations, RWC started experiencing fevers and infections that ultimately aggravated his underlying metabolic condition. (*Id.*) Lastly, Dr. Lopez responded to the third question by stating that--

> it is important to remember that the primary function of the mitochondria is that of oxidative metabolism, or energy production. The brain depends highly on oxidative metabolism and quickly becomes symptomatic when oxidative metabolism is impaired. * * *Catabolic stress, such as infections and fever, when energy demands are higher than in the normal, physiological state, are normally overcome by healthy mitochondria, but in the case of [RWC], and due to his metabolic deficiencies that is not the case; and in the background of constant fevers as a side-effect of the vaccines given to him on 14 November, 2005 his

> brain metabolic demands were not met and as a consequence of poor energy production he has shown the clinical picture that has already been mentioned. (*Id.*)

Dr. Lopez testified specifically that the mitochondrial deficiencies were not due to the vaccines RWC received, since he was born with these deficiencies. (Tr. 113.) However, Dr. Lopez believed that given his knowledge of mitochondria and how they work, "any febrile episode, any infection that produces an excess of metabolic demands on the system may unmask one of these conditions or, if it is already there, make it worse." (*Id.*)

B. Respondent's experts

1. Dr. Mark Sheldon Korson

Dr. Mark Sheldon Korson received an undergraduate degree from the University of Toronto. (Ex. B, p. 1; Tr. 153.) Dr. Korson graduated from the University of Toronto in 1982 with a degree in medicine. (*Id*.) From 1982 to 1983, Dr. Korson held a rotating internship at St. Joseph's Health Center in Toronto, Canada. (*Id*.) From 1983 to 1986, he completed his residency training in Pediatrics at the Hospital for Sick Children in Toronto. (Ex. B, p. 1; Tr. 153.) From 1986-1990, he received a Fellowship in Genetics at the Children's Hospital in Boston, Massachusetts. (*Id*.)

Dr. Korson was certified by the Medical Council of Canada in 1982 and the National Board of Medical Examiners. (Ex. B, p. 1; Tr.154.) In 1989, Dr. Korson was certified by the American Board of Pediatrics and the Royal College of Physicians of Canada. (Ex. B, p.1.) In 1993, Dr. Korson was certified by the American Board of Medical Genetics, Clinical Genetics, and Clinical Biochemical Genetics. (Ex. B, p. 1; Tr. 154.) In 1997, he was certified by the American Board of Pediatrics and recertified in 2002. (*Id.*) In 2003, he was certified by the American Board of Medical Genetics, Clinical Genetics and Clinical Biochemical Genetics; he was recertified in 2006 and 2010. (*Id.*)

Dr. Korson was appointed instructor in Pediatrics at the Harvard Medical School in Boston, Massachusetts from 1990 to 1998. (Ex. B, p. 1.) From 1998 to 2000 he was Assistant Professor of Pediatrics at Harvard Medical School in Boston, and from 2001 to the present, he has served as Associate Professor of Pediatrics at Tufts University School of Medicine. (*Id.*) Currently, Dr. Korson works as the Chief of the Metabolism Service within the Division of Genetics and Metabolism at The Floating Hospital for Children at the Tufts Medical Center. (Ex. B, p. 1; Tr. 153.)

Dr. Korson was awarded the Loewen, Ondaatje, McCutcheon & Co. Educational Award for Excellence in Clinical Teaching in 1986, the Young Investigator Award from the Society for Inherited Metabolic Disease in 1988, and the Excellence in Teaching Award, from Tufts University School of Medicine in 2003. (Ex. B, p. 2.) Dr. Korson has 35 refereed articles, 15 peer-reviewed book chapters, and 17 abstracts, listed on his CV. (*Id.*, pp. 5-8.)

2. Dr. Max Wiznitzer

Dr. Wiznitzer attended the Northwestern University Honors Program and specialized in Medical Education, earning a Bachelor of Science degree in Medicine in 1975. (Ex. D, p.1.) Dr. Wiznitzer graduated from the Northwestern University Medical School in 1977 with a degree in medicine. (*Id.*) During his postgraduate training, Dr. Wiznitzer was a resident in pediatrics at the Children's Hospital Center in Cincinnati, Ohio from 1977 to 1980. (*Id.*) He also was a fellow in developmental disorders at the Cincinnati Center for Developmental Disorders from 1980 to 1981. (*Id.*) He thereafter became a fellow in pediatric neurology at the Children's Hospital from 1981 to 1984. (*Id.*) He received the NIH National Research Service Award fellowship in Higher Cortical Functions from 1984 to1986. (*Id.*, p. 3.) From 1986 to the present, Dr. Wiznitzer has rotated between Assistant Professor of Pediatrics, Neurology, and International Health at Case Western Reserve University. (Ex. D, p. 2; Tr. 200.)

Dr. Wiznitzer has additionally won the NIG National Research Service Award from the Albert Einstein College of Medicine in1986, and was recognized as the Professional of the Year from the Autism Society of Ohio in 1991. (Ex. D, p.3.) He was certified by the American Board of Pediatrics in 1982, the American Board of Psychiatry and Neurology in Child Neurology in 1986, and the National Board of Medical Examiners in 1978. (Ex. D, p. 5; Tr. 199.) He has been licensed in Ohio (1979), Pennsylvania (1981), and New York (1984). (Ex. D, p. 5.) Dr. Wiznitzer served on the Editorial Board of many journals, including Pediatric Neurology, Journal of Child Neurology, and Lancet Neurology. (*Id.,* p. 6.) He has helped author 58 original articles, 11 book chapters, and 55 abstracts, which are listed on his CV. (*Id.*, pp. 13-23.)

3. Summary of opinions of Respondent's experts

1. Dr. Korson

Dr. Korson testified that there is insufficient evidence to diagnose RWC with a mitochondrial disorder. (Ex. A, p. 6; Tr. 183.) Dr. Korson opines that even if RWC had a mitochondrial disorder, there is insufficient evidence that the MMR or Varivax vaccine exacerbated that underlying mitochondrial disorder, causing an injury. (Ex. A, p.6; Tr. 185.) Dr. Korson's opinion is based on many different factors, including insufficient evidence to confirm a diagnosis of mitochondrial disease in this patient; the lack of a clinical phenotype consistent with a patient with a mitochondrial disorder; the lack of a temporal relationship between the immunization and the onset of developmental issues; and the lack of a causative relationship between the immunization and the patient's speech delays. (Ex. A, p.6.)

2. Dr. Wiznitzer

Dr. Wiznitzer testified that Dr. Lopez's opinion is not supported by the contemporaneous medical records. (Ex. C, p. 6.) Dr. Wiznitzer opined that RWC had features of ASD prior to his immunizations in question, had no regression of skills following any immunization, and does not have enough clinical or laboratory findings to support the diagnosis of a mitochondrial disorder. (Ex. C, p. 7; Tr. 210-214.)

VI

RESPONDENT'S EXPERTS WERE FAR MORE PERSUASIVE IN GENERAL

For all of the reasons set forth in this section and in the sections of this Decision below, I conclude that Petitioners have *failed* to demonstrate that it is "more probable than not" that RWC's vaccinations of November 14, 2005, played *any role* in causing or aggravating his ASD. And the first of the reasons for this conclusion is simply that I found Respondent's experts, Drs. Korson and Wiznitzer, to be far more persuasive than Petitioners' expert, Dr. Lopez.

A. Qualifications

In this regard, I start with the qualifications of the opposing experts relative to the issues raised by Petitioners' claim. In short, the credentials of Respondent's experts are vastly superior. Although the parties agree that RWC has an Autism Spectrum Disorder, the question in this case is whether the extent of that condition was a result of a regression resulting from an aggravation of an underlying mitochondrial disorder, as Petitioners allege, or the onset of ASD unrelated to any other condition, as Respondent contends. Petitioners relied on a single expert, Dr. Lopez, who was presented as an expert in neurology. (Tr. 98.) Respondent relied on two experts . Dr. Wiznitzer was presented not only as an expert in pediatric neurology, but also as an expert in Autism Spectrum Disorders in particular. (Tr. 204.) Dr. Korson was presented as an expert in both metabolic diseases and mitochondrial disorders. (Tr. 157.) Drs. Wiznitzer and Korson are *far* more qualified to assess the onset of RWC's ASD and to determine whether he in fact suffers from a mitochondrial disorder.

1. Expertise in autism spectrum disorders

Dr. Wiznitzer has extensive experience in diagnosing and assessing ASDs. Children with ASDs make up one of the two largest groups of patients in his clinical practice. (Tr. 202.) During the course of his clinical practice, Dr. Wiznitzer has seen thousands of children with ASD. (*Id*.) As a faculty member at Case Western Reserve University, he regularly lectures on ASDs. (Tr. 200.) In 1989, he was part of a group working on "screening, diagnosis and assessment of autism" with the National Institutes of Health, leading to the publication of a paper in the *Journal of Autism and Developmental Disorders*. (Tr. 202.) He is currently a member of the Autism Subcommittee of the American Academy of Pediatrics, and is the Pediatrics liaison for the Autism Treatment Network. (Tr. 203.) He is also working on a committee at the American Academy of Neurology putting together "guidelines for the management of autism spectrum disorders." (*Id*.) Dr. Wiznitzer has published five articles on the assessment and evaluation of ASDs. (Tr. 204.)

In contrast, although Dr. Lopez is also a pediatric neurologist with a clinical practice (Tr. 96-97), nothing in his curriculum vitae or his hearing testimony offers any indication of expertise particular to ASDs. Rather, Dr. Lopez testified that most of his clinical practice is devoted to stroke and headache patients. (Tr. 97.) His *curriculum vitae* further demonstrates this focus. (Ex. 52.) All of Dr. Lopez's listed research experience is devoted to topics pertinent to strokes, migraines, and seizures (*id*., pp. 4-10), as are most of his publications and oral presentations (*id*., pp. 11-15). There is no mention of ASDs in Dr. Lopez's *curriculum vitae*.

2. Expertise in mitochondrial disorders

Dr. Korson has been working in the field of genetics and metabolism since 1990. (Tr. 154). He is board-certified in pediatrics, clinical genetics, and biochemical genetics, which encompasses mitochondrial disorders. (*Id*.) He is a member of The Society of Inherited Metabolic Disease, the American Academy of Developmental Medicine and Dentistry, and was a founding member of the Mitochondrial Disease Action Committee ("MitoAction"). (Tr. 154-55.) Dr. Korson currently sits on the medical advisory board for MitoAction, and was commissioned by that organization to write a symptom guide for mitochondrial disease. (*Id*.) In addition to teaching about mitochondrial disease as the Director of Metabolic Services at Tufts, he spent four years on a Metabolic Outreach Service project which he developed, giving regular talks about metabolic and mitochondrial disease at five different teaching hospitals. (Tr. 155.) Dr. Korson also maintains a clinical practice in which most of his patients, two-thirds of whom are children, suffer from some form of mitochondrial disease. (Tr. 156.) Dr. Korson has published about ten articles on mitochondrial disease. (Tr. 157.)

Dr. Lopez, in contrast, acknowledged that he sees "very few" patients with mitochondrial conditions in his practice, and that he does not treat these patients. (Tr. 133.) Dr. Lopez is not board-certified in biochemical genetics, nor has he ever done any research on mitochondrial disorders. (*Id*.) Dr. Lopez's only stated experience with mitochondrial disorders stems from his participation in a presentation of several cases of mitochondrial disease at a meeting in New Orleans while he was in training as a resident at the University of South Alabama. (Tr. 134.) While this presentation ultimately led to a published abstract, Dr. Lopez himself characterized the abstract as "not really that important," and indeed, couldn't even remember the title. (*Id*.)

A particular point of disagreement between Dr. Lopez and Dr. Korson is the proper scoring of RWC's condition under the Nijmegen test, a set of clinical criteria used to determine the presence of a mitochondrial disorder. Significantly, Dr. Korson uses this test in his clinical practice (Tr. 166), while Dr. Lopez acknowledged that he was not familiar with the Nijmegen clinical criteria prior to his involvement in this case (Tr. 149).

B. Deficiencies in Dr. Lopez's testimony

Even more important than the vast gap in *qualifications* between Dr. Lopez and Respondent's experts, was the even greater gap in the experts' *ability to explain* their opinions. The written reports and hearing testimony of both Drs. Wiznitzer and Korson seemed to me to be coherent and logical. In contrast, the written reports of Dr. Lopez were short and not well explained, while his hearing testimony was often self-contradictory, and unsubstantiated by scientific explanation. In his testimony and his reports, Dr. Lopez failed to persuasively address questions critical to his causation theory. For the reasons discussed in Section VII below, I find that Petitioners have failed to establish that it is "more probable than not" that RWC suffered a mitochondrial disorder, but even setting that aside, I find as a threshold issue that Dr. Lopez has *failed* to present an adequate or even coherent basis for claiming that RWC's MMR or Varivax vaccinations caused any of his fevers, or that RWC suffered an autistic regression as a result of his vaccinations.

1. Dr. Lopez has not substantiated his assertion that RWC suffered a fever caused by his MMR or Varivax vaccinations

In his initial report, Dr. Lopez was entirely vague about the timing of the alleged symptom-provoking fever or fevers, stating only that his opinion was supported by fever episodes which occurred "shortly" after the vaccinations. (Ex. 51, p. 2.) In a supplemental report, having been specifically asked to identify the time when the febrile episodes at issue had occurred, Dr. Lopez stated "approximately two weeks" after the vaccinations in question. (Ex. 53, p. 2.) Only after respondent's expert, Dr. Korson, contended in his report that the first *documented* fever (which occurred in late December more than a month following the vaccination) was too remote to be linked to the November 14 vaccinations (Ex A, p. 5), did Dr. Lopez later submit a second supplemental report indicating for the first time that his cause-in-fact opinion was based on the fact that "Ms. Coombs told me that [RWC] developed a fever the same day his vaccines were given on 14 NOV 2005"[8] (Ex. 55, p. 3).

At the evidentiary hearing, Dr. Lopez asserted that the expected timeframe for developing a fever after an MMR vaccination would be "one, two or three days at most." (Tr. 116.) Dr. Lopez offered that a fever may occur "sometimes the same afternoon or the following morning." (*Id*.) Asked how far out one can go and attribute a fever to a vaccine, Dr. Lopez responded that "I think that after the fourth, fifth day probably it's unlikely that the vaccine gave the patient a fever probably." (Tr. 116-17.) On cross-examination, however, Dr. Lopez's attention was drawn to a Centers for Disease Control (CDC) "MMR Vaccine Information Sheet" attached to *his own* second supplemental report in the Coombs case. (Tr. 117.) That MMR information sheet indicates that if problems such as fever occur, "it is usually within 7-12 days after the shot." (Ex. 55, p. 6.) Initially Dr. Lopez refused to disagree with the statement made in the vaccine information sheet, but when specifically asked about the contradiction between his prior testimony and his reliance on the MMR information sheet, Dr. Lopez stated that "I know that they put this here, but usually what I have seen in my years, the fever usually happens shortly after the vaccine, not two weeks after." (Tr. 119.)

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[8] Petitioners devote much attention in their post-hearing brief to the question of whether or not Ms. Coombs's testimony regarding the November 14 fever is to be believed. (ECF No. 71, pp.11-12; ECF No. 77, pp. 4-5.) For the reasons discussed in this section, resolution of that question is not necessary to the conclusion I have reached. Nonetheless, it is worth noting that Dr. Lopez's ultimate opinion in this case appears to be predicated entirely on attributing the fever that RWC allegedly suffered on November 14, 2005, to the administration of RWC's MMR and Varivax vaccinations. Dr. Lopez agreed not only that RWC's first *documented* fever occurred on December 18, 2005 (Tr. 135), but also that the December 18 fever was too remote in time to have been caused by RWC's November 14 vaccinations (Tr. 120). And although Ms. Coombs offered testimony indicating that she believed that RWC experienced another fever around December 6 or 8 (Tr. 24), Dr. Lopez did not specifically acknowledge that fever in his reports or testimony, and at no point linked it in any way to RWC's vaccinations. In any event, a fever occurring at about that time (Dec. 6-8) would not be attributable to RWC's November 14 vaccinations according to Dr. Lopez's own testimony, discussed further below, indicating that after five days a fever could not be readily attributable to a prior vaccination. (Tr. 116-17.)

Significantly, the timeframe indicated by the MMR information sheet is consistent with Dr. Lopez's first supplemental report, but in conflict with his second supplemental report and hearing testimony. That is, in his first supplemental report, Dr. Lopez asserted that RWC's initial fever, which he believed at that point to have occurred two weeks following the November 14 vaccinations, was attributable to those vaccinations. (Ex 53.) At the hearing, however, after he had clarified with Ms. Coombs his understanding of the timing of RWC's initial fever (Tr. 120-21), he directly contradicted that earlier opinion and testified that a fever cannot be attributed to a vaccine after about five days. (Tr. 116-17.) Despite the contradiction, Dr. Lopez confusingly testified that he stands by *all three* of his reports. (Tr. 115.)

Thus, on this critical question, Dr. Lopez has offered self-contradictory testimony at odds with his own prior reports. He offered no explanation for his change of opinion as to whether an MMR-caused fever should take one day or two weeks to develop, and he has failed to explain or substantiate his ultimate opinion that vaccines can cause a fever within twenty-four hours, other than by unspecified anecdotal instances allegedly having occurred in his own practice. Under these circumstances, Dr. Lopez's opinion on this subject simply cannot be credited.[9] *See, e.g. Knudson v. HHS*, 35 F.3d 543, 548 (Fed. Cir. 1994)(holding that under the Vaccine Act, the "'logical sequence of cause and effect' must be supported by a sound and reliable medical or scientific explanation"); *see also Caves v. HHS*, 100 Fed. Cl. 119, 134 (2011), *aff'd* 463 F. App'x 932 (Fed. Cir. 2012)(quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136 (1997) for the

[9] In contrast to Dr. Lopez' views, respondent's expert, Dr. Wiznitzer, did describe the basis for his expert opinion that the one-to-two week period reflected in the MMR vaccination information sheet is accurate. (Tr. 217.) Dr. Wiznitzer persuasively explained that "the way that the vaccine promotes the production of protective antibodies is by the viruses replicating, but in a controlled fashion, and therefore provoking an immune response." (Tr. 216.) Based on this process, and comparing it to the incubation period when someone contracts the wild measles virus, he contended that it is "biologically impossible" for an attenuated virus vaccine to create a fever within one day. (*Id*.) Thus, Dr. Wiznitzer testified that if RWC experienced a fever on or about November 14, 2005, it more likely than not would have been caused by something other than the vaccination. (Tr. 217.) In addition, respondent's other expert, Dr. Korson, cast further doubt on Dr. Lopez's reliance on a fever on November 14, 2005, as an event triggering an onset of mitochondrial disorder symptoms. Dr. Korson testified that aggravation of any underlying mitochondrial disorder would involve weeks of "profound" fatigue "as if their system is down for several weeks until they slowly recover." (Tr. 185.) Noting that RWC's medical records for his physician visit of December 1, 2005, characterized him as "healthy appearing, happy and extremely active," Dr. Korson testified that this notation is not consistent with what he would expect if RWC had experienced aggravation of a mitochondrial disorder through a febrile episode two weeks earlier. (Tr. 186.) Significantly, Dr. Korson attributes RWC's first documented fever of December 18 to an upper respiratory infection (Ex A, p. 5) which Dr. Lopez agrees could cause exactly the kind of metabolic stress condition he asserts caused RWC's autistic regression, testifying that "a fever is a fever" in terms of its ability to unmask an underlying mitochondrial disorder. (Tr. 135.) Thus, even assuming that the fever did occur on November 14, I would still find Respondent's experts *far* more convincing on the question of whether that fever could be linked to RWC's vaccinations.

proposition that "*Daubert* does not require a trial court 'to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert.'").

2. Dr. Lopez has not substantiated his assertion that RWC suffered an autistic regression following his MMR and varivax vaccinations

Dr. Lopez testified that he could not say what RWC's first ASD symptom was (Tr. 123), but he acknowledged that RWC exhibited oral and texture aversion as a symptom of his ASD, symptoms which *predated* his vaccinations (Tr. 124). He also acknowledged that medical records indicate that RWC also exhibited *speech delay* prior to his vaccinations. (Tr. 105-06.) And while he attributed that speech delay to hearing problems, he acknowledged that speech delay is a sign of ASD. (Tr. 124.) Nonetheless, Dr. Lopez seemed to assert, without coherent explanation, that what RWC experienced prior to the vaccinations in question was *not* the onset of ASD, but that instead RWC experienced developmental regression *following* his vaccinations in question (Tr. 107-08); for example, he stated in his initial expert report that "this child was developing just fine until shortly after he received his scheduled immunizations." [10] (Ex. 51, p. 3).

Dr. Lopez could not explain when the alleged regression in development occurred beyond noting that it was "sometime after" the vaccinations. (Tr. 125-26.) Nor could he point to any medical records where regression was indicated. (Tr. 126.) Rather, Dr. Lopez testified that his opinion that a regression occurred was based on Ms. Coombs's representation to him that "[RWC] was developing normally" prior to his vaccination. (Tr. 125.) Even taking this statement at face value, however, it does not by itself establish that RWC experienced a regression (*i.e.*, a *loss* of developed skills) as opposed to the type of ongoing clinical onset of autism suggested by Dr. Wiznitzer. Nor is it consistent with Dr. Lopez's above-referenced acknowledgment that RWC exhibited signs of autism prior to his vaccination. In fact, Dr. Lopez indicated that prior to speaking directly with Ms. Coombs he was not sure based on the medical records whether RWC was "normal or not before the vaccine." (Tr. 105.)

In this regard, Ms. Coombs's testimony that she did not closely track or document RWC's early developmental milestones, and could not remember them with specificity, is significant. (Tr. 17-18, 63.) Although she stated that she did not have any reason for concern regarding RWC's development prior to his 16-month vaccinations (Tr. 65), Dr. Wiznitzer explained that the signs of ASDs are "very subtle" until about 18 to 24 months of age, because

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[10] In contrast, Dr. Wiznitzer explained that oral and texture aversion "is a well-known behavior described in this population and seen in infancy in children who later evolve into autism spectrum disorders," and stated that in light of RWC's subsequent ASD diagnosis "it's obvious that that was an early manifestation of that presentation." (Tr. 207-08.) Dr. Wiznitzer also discussed notations in RWC's medical records indicating that RWC could count to ten by either age nine months or seventeen months. Such behavior, Dr. Wiznitzer indicated, "is not normal childhood behavior. If it's present, it implies that it's probably repeating what other people are saying and it does not have any true meaning to it." (Tr. 229-30.) Dr. Wiznitzer explained that this behavior, called "echolalic behavior," can be considered a symptom of autism. (Tr. 230). In fact, Dr. Wiznitzer indicated that where a child's first words are counting without other "good functional speech," that is an "early marker of an ASD." (Tr. 231.)

the social and communicative behaviors that ASDs impact do not really develop until that time. Therefore, the dysfunction is not apparent prior to that time. (Tr. 210-11.) Dr. Wiznitzer stated that it is "very difficult" to identify children with ASD at six months, and that detecting ASD at twelve months would require the observer to be "very attuned." (*Id*.) Asked whether the early signs of ASD are subtle enough to be missed during developmental screening, Dr. Wiznitzer responded, "the answer is clearly yes." (Tr. 214.)

After extensive recitation of RWC's medical history, Dr. Wiznitzer, who as described above is much better qualified than Dr. Lopez to assess the course of RWC's ASD onset, opined both in his expert report and at the hearing that RWC presented a clinical course that is "consistent with the trajectory of ASD's presentation," and that there is "no history in the contemporaneous medical records of a regression in his development." (Ex. C, p. 6; *see also, e.g.*, Tr. 227.)

C. ***Conclusion***

The above deficiencies in Dr. Lopez's testimony, particularly when compared against Dr. Wiznitzer's and Dr. Korson's superior qualifications and much more detailed and coherent explanations, leave Petitioners unable to demonstrate either that RWC experienced a fever that was triggered by his vaccinations, or that RWC experienced a post-vaccination regression. These deficiencies are therefore fatal to Petitioners' claim in themselves. Nonetheless, as detailed in the section below, I also find based on the evidence before me that Petitioners have failed to show that it is "more probable than not" that RWC suffers an underlying mitochondrial disorder.

VII

THE EVIDENCE DOES NOT SUPPORT A CONCLUSION THAT RWC SUFFERED FROM A MITOCHONDRIAL DISORDER

In 2009, RWC was referred to Dr. John Shoffner of MNG Medical Neurogenics to be tested for a possible mitochondrial disorder. (Tr. 50-51.) Dr. Shoffner conducted three types of assessment: clinical scoring (according to the "Nijmegen Clinical Criteria for Mitochondrial Diseases"); biochemical criteria scoring; and genetic criteria scoring. (Ex. 37, p. 2230; *see also* Tr. 133.) On the whole, although he noted Complex I and Complex III deficiencies within the biochemical test results and "isolated involvement of the central nervous system" within the clinical scoring, Dr. Shoffner found *insufficient* evidence to diagnose RWC with a mitochondrial disorder. (Ex. 37, p. 2230.) There does not appear to be any dispute as to the validity of Dr. Shoffner's testing. In fact, Petitioners' expert relies on these test results in his second supplemental report. (*See* Ex. 55, p. 2.) Rather, Petitioners' position that RWC suffers from a mitochondrial disorder is based on (1) accepting the Complex I and Complex III deficiencies found by Dr. Shoffner as being definitive of a mitochondrial disorder diagnosis; (2) rescoring Dr. Shoffner's clinical assessment under the Nijmegen criteria to show a greater likelihood of a disorder; and (3) relying on RWC's presentation of developmental delay as a clinical sign of a mitochondrial disorder.

A. Biochemical and genetic criteria scoring

With regard to biochemical criteria, Dr. Lopez indicated that his opinion that RWC suffered a mitochondrial disorder was based on enzymology findings made by Dr. Shoffner that RWC suffered from "Complex I and Complex III mitochondrial deficiencies." (Tr. 111-12.) To be sure, it is not disputed in this case that Dr. Shoffner found Complex I and Complex III deficiencies in RWC's enzymology, and that Dr. Goldstein continued to treat RWC as *potentially* suffering from mitochondrial dysfunction. (*See, e.g.*, ECF No. 74, pp. 9-10.) Dr. Korson, however, explained that the discovery of the Complex I and Complex III enzymology deficiency is a "finding," and not a "diagnosis." (Tr. 177.)

According to Dr. Korson, the Complex I and Complex III deficiencies would have qualified as a diagnosis of a mitochondrial disorder back in the 1990's, but since that time scientists have discovered that there can be "any number of reasons" *not related* to the mitochondria for decreases in enzymology. (Tr. 182.) Thus, these deficiencies do not indicate that the mitochondria are "diseased, per se." (*Id*.) In this regard, despite these findings of Complex I and Complex III deficiencies, Dr. Korson and Dr. Shoffner both agreed that it was unlikely that RWC had a mitochondrial disorder. (*See* Ex. 37, p. 2230; *see also* Tr. 158.) In fact, Dr. Shoffner stated in his report that "I am NOT convinced that this patient has a mitochondrial disease. A single abnormality (abnormal enzymology) is not sufficient criteria for definitive diagnosis." [11] (Ex. 37, p. 2230 (emphasis in original).)

Dr. Korson further noted that enzymology findings can vary from lab to lab depending on the methodologies used, and indicated that the Complex I is the "most unstable" and subject to showing abnormal results due to testing errors. (Tr. 177.) For this reason, Dr. Korson explained, enzymology results are no longer relied on as "the key factor in making a diagnosis" of mitochondrial disorder. (Tr. 182.) Rather, genetic testing is done to look for abnormalities that are normally associated with Complex I and Complex III deficiencies where mitochondrial disease is present. (Tr. 177, 182.) At the time of Dr. Shoffner's report, the genetic tests remained

[11] Petitioners argue, in effect, that it is a mistake to give any weight to Dr. Shoffner's assessment. (ECF No. 71, p. 13 (stating that Respondent's reliance on Dr. Shoffner's diagnoses is "misguided").) I disagree. Petitioners stress that Dr. Schoffner's opinion was not intended as a final conclusion, that additional testing was called for, and that Dr. Shoffner never actually definitively ruled out a mitochondrial disorder. (ECF No. 71, p. 13.) Respondent's expert, Dr. Korson pointed out, however, that the subsequent testing confirmed Dr. Shoffner's skepticism. (Tr. 195-96.) In any event, even if Dr. Shoffner offered only a preliminary conclusion, this is no reason to discount his underlying clinical impressions. Petitioners also urge that Dr. Goldstein's continued treatment of RWC for a mitochondrial disorder following Dr. Shoffner's testing is "quite compelling" evidence that RWC did in fact suffer from such a disorder. (ECF No. 71, pp. 12-13.) However, to the extent that this may appear to represent a disagreement among the original clinicians, I note that Dr. Goldstein's referral of RWC to Dr. Shoffner for diagnosis was itself an act of deference to Dr. Shoffner's expertise in that area in the first place. I also note that Dr. Shoffner's opinion is persuasively supported by Dr. Korson's own reasoning. Dr. Korson, as described in Section VI(A)(2) of this Decision, is very well qualified in the diagnosis of mitochondrial disorders.

pending. (Ex. 37, p. 2230.) However, these tests later came back *negative* for these types of abnormality. (Ex. 44, pp. 10-14; Tr. 182.)

Therefore, the biochemical and genetic criteria do *not* appear to support a diagnosis of mitochondrial disorder. Although Dr. Shoffner listed such a diagnosis as "possible" under biochemical scoring based on the Complex I and Complex III deficiencies, he urged that "a definitive diagnosis is not made with a single abnormality." (Ex. 37, p. 2230.) Moreover, at the time of that writing, Dr, Shoffner did not have the benefit of the pending genetic tests. These tests, which Dr. Korson indicated were critical to confirming the significance of the biochemical results, came back negative. Thus, under these circumstances, the Complex I and Complex III findings alone do not appear to be sufficient to diagnose RWC with a mitochondrial disorder.

B. Clinical criteria scoring

In terms of clinical criteria, Dr. Shoffner scored RWC based on the "Nijmegen criteria," a compilation of various tests results and clinical observations used to determine whether sufficient signs of mitochondrial disorder exist. (Ex. 37, p. 2230.) Dr. Shoffner scored a single "point" for RWC out of a possible twelve, meaning that a mitochondrial disorder is "unlikely." (*Id*.) In his expert report Dr. Korson indicated his agreement with Dr. Shoffner's assessment under the Nijmegen criteria. (Ex. A, p. 4.) Based on his review, Dr. Lopez testified that he would re-score RWC as a six, meaning mitochondrial disorder is "probable." (Tr. 145-46.) Dr. Lopez's testimony on this issue is problematic in several regards, however, and, as a result, I do not find it credible.

First, I find that Dr. Lopez's re-scoring of the Nijmegen criteria is, at least in part, speculative. For example, Dr. Lopez agreed with Petitioners' counsel that he would add two points to RWC's Nijmegen score for having an abnormal resting metabolic rate. (Tr. 144-45.) Dr. Lopez reached this conclusion, he states, because his review of RWC's medical records led him to *expect* RWC to have an abnormal exercise study. (Tr. 145.) Dr. Korson indicated, however, that such exercise studies are generally not used for patients younger than about ten years old (Tr. 168), and Dr. Lopez admitted that no such exercise study was done in RWC's case (Tr. 144-45). In this regard even Dr. Lopez characterized *his own* scoring as "speculative." (Tr. 144-45).

Second, to the extent Dr. Lopez's re-scoring is in conflict with the assessment Dr. Shoffner recorded in the medical records, I believe Shoffner's contemporaneous clinical impression is deserving of greater weight. That is, Dr. Lopez has not convinced me of any error made by Dr. Shoffner in his assessment. For example, Dr. Lopez cites Dr. Shoffner's finding that RWC had a low carnitine level as supporting a diagnosis of mitochondrial disorder. (Ex. 55, p. 2.) Dr. Shoffner, however, appears to have discounted this possibility, noting instead that the low carnitine level is "likely of dietary origin." (Ex. 37, p. 2228.)

Dr. Korson explained that the most common sources of carnitine are red meat, milk, and dairy products, and, therefore, dietary issues are the most common cause of a low carnitine level. (Tr. 174.) Additionally, Dr. Korson noted that the ratio of free carnitine to total carnitine is an important indicator, and that RWC's ratio suggested dietary deficiency rather than metabolic disorder. (Tr. 174-75.) Dr. Korson's explanation of Dr. Shoffner's decision to discount the low

carnitine level is supported by the medical records. The lab report prepared for Dr. Shoffner in RWC's case indicated a normal ratio and a likely dietary deficiency. (Ex. 37, p. 2208.) Dr. Lopez, on the other hand, testified that he did not know what the most common cause of low carnitine was, or why Dr. Shoffner concluded that RWC's low carnitine was of dietary origin. (Tr. 151.)

Finally, Dr. Lopez has no prior clinical experience applying the Nijmegen criteria, while Dr. Shoffner's assessment is affirmed by Dr. Korson, who, in addition to being well-qualified in this area, has prior clinical experience applying the Nijmegen test criteria in particular. This lends greater weight to Dr. Korson's assessment of the Nijmegen factors. For example, Dr. Lopez reached his conclusion in part by adding two points onto Dr. Shoffner's scoring of the Nijmegen scale, because RWC's tests revealed an elevated lactate level. (Tr. 144.) Dr. Korson explained, however, that lactate can be elevated for a number of reasons, the most common of which is an error in processing the test. (Tr. 169-70, 179, 189-90.) For this reason, Dr. Korson indicated that in order to find that lactate is "truly" elevated, it is necessary to confirm an elevated lactate level by also finding elevated alanine and organic acids. (Tr. 170-71, 173, 189-90.) Because there was no elevated alanine or organic acid in this case, Dr. Korson believed that Dr. Shoffner was correct to discount the finding of elevated lactate in RWC's case. (Tr. 189-90.) Dr. Lopez, however, appeared to be unaware of this method of confirmation. (Tr. 151.)

C. RWC's developmental delay as a clinical presentation of mitochondrial disorder

Dr. Lopez relies on RWC's developmental delay as primary evidence of RWC's clinical presentation of mitochondrial disorder, arguing that it is evidence that the mitochondrial disorder has impacted his brain. (Tr. 127-28.) And, to be sure, Dr. Korson acknowledged that RWC's developmental delay was the basis for the one point that Dr. Schoffner did score on RWC's Nijmegen assessment. (Tr. 178). Dr. Lopez acknowledged, however, that although he believed RWC's developmental delay was "consistent" with mitochondrial disorder, it could also be explained as part of his autism. (Tr. 128) That is, Dr. Lopez admitted that someone could have the same symptoms as RWC and *not* have a mitochondrial disorder. (*Id*.)

Dr. Korson, on the other hand, though he acknowledged RWC's ASD diagnosis, indicated that in terms of being evidence of a mitochondrial disorder, it is "not a very specific finding," because "any kind of developmental issue has been described with mitochondrial disease." (Tr. 183.) Dr. Korson indicated that there is no "specific presentation" for a patient with Complex I or Complex III deficiencies, but based on his review of the records, Dr. Korson did not believe that RWC had any features associated with energy issues. (*Id*.) Dr. Korson indicated that "an isolated brain problem" without "other organ systems involved" would be unusual. (Tr. 180.)

D. Conclusion

On the whole Dr. Lopez has failed to convince me that his re-scoring of Dr. Shoffner's clinical assessment is either sufficiently grounded in RWC's medical history, or more accurate than Dr. Shoffner's original assessment. Absent that re-scoring, he has also failed to demonstrate that RWC's ASD on its own is a sufficient clinical marker of a mitochondrial disease. Additionally, Complex I and Complex III deficiencies without genetic confirmation

likewise do not appear to be an adequate marker of a mitochondrial disorder where the clinical picture is otherwise lacking. For these reasons, I find that Petitioners have *failed* to demonstrate that it is "more probable than not" that RWC suffered an underlying mitochondrial disorder.

VIII

PETITIONERS' CASE FAILS THE ALTHEN TEST

As noted above, in its ruling in *Althen*, the U.S. Court of Appeals for the Federal Circuit discussed the "causation-in-fact" issue in Vaccine Act cases. The court stated as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between the vaccination and injury. If Althen satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F.3d 1274, 1278 (Fed. Cir. 2005)(citations omitted). In the pages above, of course, I have already set forth in detail my analysis in rejecting Petitioners' "causation-in-fact" theory in this case. In this part of my Decision, then, I will briefly explain how that analysis fits specifically within the three parts of the *Althen* test, enumerated in the first sentence of the *Althen* excerpt set forth above. The short answer is that I find that Petitioners' theory in this case clearly does not satisfy the *Althen* test.

A. Relationship between Althen Prongs 1 and 2

One interpretive issue with the *Althen* test concerns the relationship between the first two elements of that test. The first two prongs of the *Althen* test, as noted above, are that the petitioners must provide "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury." Initially, it is not absolutely clear how the two prongs differ from each other. That is, on their faces, each of the two prongs seems to require a demonstration of a "causal" connection between the "vaccination" and "the injury." However, a number of Program opinions have concluded that these first two elements reflect the analytical distinction that has been described as the "can cause" vs. "did cause" distinction. That is, in many Program opinions issued prior to *Althen* involving "causation-in-fact" issues, special masters or judges stated that a petitioner must demonstrate (1) that the *type* of vaccination in question *can* cause the *type* of injury in question, and also (2) that the *particular* vaccination received by the specific vaccine *did* cause the vaccinee's *own* injury. *See, e.g., Kuperus v. HHS*, 2003 WL 22912885, at *8 (Fed. Cl. Spec. Mstr. Oct. 23, 2003); *Helms v. HHS*, 2002 WL 31441212, at *18 n. 42 (Fed. Cl. Spec. Mstr. Aug. 8, 2002). Thus, a number of judges and special masters of this court have concluded that Prong 1 of *Althen* is the "can cause" requirement, and Prong 2 of *Althen* is the "did cause" requirement. *See, e.g., Doe 11 v. HHS*, 83 Fed. Cl. 157, 172-73 (2008); *Nussman v. HHS*, 83 Fed. Cl. 111, 117 (2008); *Banks v. HHS*, 2007 WL 2296047, at *24 (Fed. Cl. Spec. Mstr. July

20, 2007); *Zeller v. HHS*, 2008 WL 3845155, at *25 (Fed. Cl. Spec. Mstr. July 30, 2008). And, most importantly, the *Federal Circuit* confirmed that interpretation in *Pafford*, ruling explicitly that the "can it?/did it?" test, used by the special master in that case, was equivalent to the first two prongs of the *Althen* test. *Pafford v. HHS*, 451 F.3d at 1352, 1355-56 (Fed. Cir. 2006). Thus, interpreting the first two prongs of *Althen* as specified in *Pafford*, under Prong 1 of *Althen* a petitioner must demonstrate that the type of vaccination in question can cause the type of condition in question; and under Prong 2 of *Althen* that petitioner must then demonstrate that the particular vaccination did cause the particular condition of the vaccinee in question.

Moreover, there can be no doubt whatsoever that the *Althen* test ultimately requires that, as an overall matter, a petitioner must demonstrate that it is "more probable than not" that the particular vaccine was a substantial contributing factor in causing the particular injury in question. That is clear from the statute itself, which states that the elements of a petitioner's case must be established by a "preponderance of the evidence." § 300aa-13(a)(1)(A). And, whatever is the precise meaning of Prongs 1 and 2 of *Althen,* in this case the overall evidence falls far short of demonstrating that it is "more probable than not" that any of the vaccines that RWC received contributed to the causation of RWC's tragic neurodevelopmental disorder.

B. Petitioners have established Prong 1 of Althen in this case

As explained above, under Prong 1 of *Althen* a petitioner must provide a medical theory demonstrating that the *type* of vaccine in question can cause the *type* of condition in question. Petitioner's theory is that a fever caused by RWC's MMR and/or Varivax vaccinations provoked an autistic regression, by unmasking an underlying mitochondrial disorder. In this case, Respondent's expert agreed that a fever is *capable* of aggravating an underlying mitochondrial disorder and causing autistic regression. (*See, e.g.*, Tr. 239-40.) At least for the purposes of this case, then, it would seem that Petitioners have satisfied the first *Althen* prong--*i.e.*, the evidence in this case preponderates in favor of the theory that a fever is capable of aggravating an underlying mitochondrial disorder, thereby causing an autistic regression.[12]

C. Petitioners have failed to establish Prong 2 of Althen in this case

Under Prong 2, the Petitioners need to show that it is "more probable than not" that one of RWC's vaccinations *did* cause RWC's *own* severe neurodevelopmental disorder. But this they have failed to do, for all of the reasons detailed above. Again, Petitioners' theory is that a fever caused by RWC's MMR and/or Varivax vaccinations provoked an autistic regression by unmasking an underlying mitochondrial disorder. Yet Petitioners have failed to persuasively establish that any of RWC's fevers could be attributed to his vaccinations (*see* Section VI (B)(1)

[12] It is worth noting, however, that Dr. Lopez acknowledged at the hearing that in order for this theory *to apply in this case,* RWC must have had an underlying mitochondrial disorder and experienced a fever caused by his MMR and/or Varivax vaccinations. (Tr. 116). Because, as discussed in Section VIII (C) of this Decision below, I find that these factual predicates have *not* been established in this case, the medical theory advanced by Petitioners, even if undisputed, remains a complete mismatch to the record of this case. Therefore, satisfaction of the first *Althen* prong in this case is effectively rendered academic, since Petitioners *failed*, as explained above, to establish Prongs 2 and 3 of the *Althen* test.

above); that he experienced any autistic *regression* at all (*see* Section VI(B)(2) above); or that he actually had an underlying mitochondrial disorder (*see* Section VII above). Thus, Petitioners have failed to establish Prong 2 of *Althen* in this case.[13]

D. Petitioners have failed to establish Prong 3 of Althen in this case

Since I have explained why Petitioners have failed to satisfy the *second* prong of *Althen*, I need not discuss why Petitioners' case also fails to satisfy the *third* prong. However, I will note again Dr. Lopez's inability to coherently identify a time period during which a fever can be attributed to a vaccination; his inability to identify the timeframe during which the alleged autistic regression occurred; and his admission that RWC exhibited symptoms of autism prior to his vaccinations. These deficiencies in Dr. Lopez's testimony would preclude any finding of a proximate temporal relationship between the vaccination and the injury, as required under *Althen* Prong 3.

E. This is <u>not</u> a close case

As noted above, in *Althen* the Federal Circuit indicated that the Vaccine Act involves a "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." 418 F.3d at 1280. Accordingly, I note here that this case ultimately is *not* a close case. For all the reasons set forth above, I found that Dr. Lopez's theory was *not at all* persuasive, while Respondent's experts were *far* more persuasive.

IX

CONCLUSION

The record of this case demonstrates plainly that RWC and his family have been through a tragic ordeal. I had the opportunity, in the courtroom during the evidentiary hearing, to meet and observe RWC's mother. I have also studied the records describing RWC's medical history, and the efforts of his family in caring for him. Based upon those experiences, the great dedication of RWC's family to his welfare is readily apparent to me.

Nor do I doubt that RWC's parents are sincere in their belief that vaccines played a role in causing RWC's *autism*. RWC's parents have heard the opinion of Dr. Lopez, and likely other physicians who profess to believe in a causal connection between vaccines and autism. After studying the extensive evidence in this case, I am convinced that the opinions provided by the petitioners' expert in this case, advising the Coombs family that there is a causal connection between vaccines and RWC's autism, have been *quite wrong*. Nevertheless, I can understand why RWC's parents found such opinions to be believable under the circumstances. I conclude that the Petitioners filed this Program claim in good faith.

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[13] To clarify, Petitioners have failed to show that RWC's autism was either *initially caused* by his vaccinations, or was aggravated in any way by his vaccinations.

Thus, I feel deep sympathy for the Coombs family. Further, I find it unfortunate that my ruling in this case means that the Program will not be able to provide funds to assist this family, in caring for their child who suffers from a serious disorder. It is my view that our society does not provide enough assistance to the families of *all* autistic children, regardless of the cause of their disorders. And it is certainly my hope that our society will find ways to ensure that in the future *much* more generous assistance is available to all such children. Such families must cope every day with tremendous challenges in caring for their autistic children, and all are deserving of sympathy and admiration. However, I must decide this case not on sentiment, but by analyzing the evidence. Congress designed the Program to compensate only the families of those individuals whose injuries or deaths can be linked causally, either by a Table Injury presumption or by a preponderance of "causation-in-fact" evidence, to a listed vaccine. In this case, the evidence advanced by the petitioners has fallen far short of demonstrating such a link. Accordingly, I conclude that the petitioners in this case are *not* entitled to a Program award on RWC's behalf.[14]

/s/ George L. Hastings, Jr.
George L. Hastings, Jr.
Special Master

[14] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.